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     4 Feb 24
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                NTIS now allows simultaneous left and right truncation
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        Mar 24
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                 PATDPAFULL now available on STN
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NEWS
                 structures available in REGISTRY
NEWS 10
        Apr 11
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NEWS 11
         Apr 14
                 MEDLINE Reload
NEWS 12
                 Polymer searching in REGISTRY enhanced
         Apr 17
NEWS 13
         Jun 13
                 Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 14
                 New current-awareness alert (SDI) frequency in
        Apr 21
                 WPIDS/WPINDEX/WPIX
NEWS 15
         Apr 28
                 RDISCLOSURE now available on STN
NEWS 16
        May 05
                 Pharmacokinetic information and systematic chemical names
                 added to PHAR
NEWS 17
         May 15
                 MEDLINE file segment of TOXCENTER reloaded
                 Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 18
         May 15
                 Simultaneous left and right truncation added to WSCA
NEWS 19
         May 19
                 RAPRA enhanced with new search field, simultaneous left and
NEWS 20
        May 19
                 right truncation
NEWS 21
         Jun 06
                 Simultaneous left and right truncation added to CBNB
NEWS 22
        Jun 06
                PASCAL enhanced with additional data
                 2003 edition of the FSTA Thesaurus is now available
NEWS 23
        Jun 20
NEWS 24
        Jun 25
                 HSDB has been reloaded
NEWS 25
                 Data from 1960-1976 added to RDISCLOSURE
        Jul 16
NEWS 26
                 Identification of STN records implemented
         Jul 21
NEWS 27
         Jul 21
                 Polymer class term count added to REGISTRY
NEWS 28
         Jul 22
                 INPADOC: Basic index (/BI) enhanced; Simultaneous Left and
                 Right Truncation available
              April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
NEWS EXPRESS
              MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
              AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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              STN Operating Hours Plus Help Desk Availability
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              Welcome Banner and News Items
NEWS PHONE
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NEWS WWW
              CAS World Wide Web Site (general information)
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FILE COVERS 1907 - 23 Jul 2003 VOL 139 ISS 4 FILE LAST UPDATED: 22 Jul 2003 (20030722/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s displacement(w)chromatography?
         89208 DISPLACEMENT
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16977 DISPLACEMENTS

101646 DISPLACEMENT

(DISPLACEMENT OR DISPLACEMENTS)

285871 CHROMATOGRAPHY?

549282 CHROMATOG

3045 CHROMATOGS

551491 CHROMATOG

(CHROMATOG OR CHROMATOGS)

643047 CHROMATOGRAPHY?

(CHROMATOGRAPHY? OR CHROMATOG) 618 DISPLACEMENT (W) CHROMATOGRAPHY?

and reductase => s l1

72580 REDUCTASE

5846 REDUCTASES

73531 REDUCTASE

(REDUCTASE OR REDUCTASES)

 L_2 2 L1 AND REDUCTASE

=> s 11 and HMG?

9072 HMG?

L3

L1

2 L1 AND MMG?

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            827 COAS
          36018 COA
                   (COA OR COAS)
          72580 REDUCTASE
           5846 REDUCTASES
          73531 REDUCTASE
                   (REDUCTASE OR REDUCTASES)
           7819 COA(W) REDUCTASE
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     ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS On STN
ACCESSION NUMBER:
                           2001:334067 CAPLUS
DOCUMENT NUMBER:
                           135:225890
TITLE:
                           Chromatographic purification of some
                           3-hydroxy-3-methylglutaryl coenzyme A
                           reductase inhibitors
                           Grahek, R. Milivojevic, D.; Bastarda, A.; Kracun, M.
Lek d.d., Research and Development, Ljubljana, 1526,
AUTHOR (S):
CORPORATE SOURCE:
                           Slovenia
                           Slovenia
Journal of Chromatography, A (2001) 918(2), 319-324
SOURCE:
                           CODEN: JCRAEY; ISSN: 0021 9673
                           Elsevier Science B.V.
PUBLISHER:
DOCUMENT TYPE:
                           Journal
LANGUAGE:
                           English
AΒ
     The purifn. of pravastatin, simvastatin and lovastatin in the sodium salt
     or lactone form and of mevastatin in the lactone form by reversed-phase
     displacement chromatog. is presented. The mobile phases
     consisted of water or mixts. of water-methanol and water-acetonitrile.
     Six different displacers were successfully used. Up to 0.14 q of raw
     sample per g of stationary phase was loaded on a column packed with
     silica-based octadecyl phase. Crude substances from 85 to 88% chromatog.
     purity were purified and at least 99.5% purity was achieved.
REFERENCE COUNT:
                           28
                                 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
     ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
                           2000:210141 CAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                           132:241979
TITLE:
                           Process for obtaining HMG-CoA reductase
                           inhibitors of high purity
INVENTOR(S):
                           Grahek, Rok; Milivojevic, Dusan; Bastarda, Andrej
                          Lek Pharmaceutical and Chemical Company D.D., Slovenia PCT Int. Appl., 25 pp.
PATENT ASSIGNEE(S):
SOURCE:
                           CODEN: PIXXD2
DOCUMENT TYPE:
                           Patent
LANGUAGE:
                           English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                       KIND DATE
                                              APPLICATION NO. DATE
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                              20000330
                                              WO 1999-IB1553
                                                                 19990917
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              DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
              KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
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MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,

MD, RU, TJ, TM

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                            20020820
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PRIORITY APPLN. INFO.:
                                        SI 1998-241
                                                         Α
                                                            19980918
                                        WO 1999-IB1553
                                                         W
                                                            19990917
     Lovastatin, pravastatin, simvastatin, mevastatin, atorvastatin, and
AB
     derivs. and analogs are known as HMG-CoA reductase inhibitors
     and are used as antihypercholesterolemic agents. The majority of them are
     produced by fermn. using microorganisms of different species identified as
     species belonging to Aspergillus, Monascus, Nocardia, Amycolatopsis, Mucor
     or Penicillium genus, some are obtained by treating the fermn. products
     using the method of chem. synthesis or they are the products of total
     chem. synthesis. The purity of the active ingredient is an important
     factor for manufg. the safe and effective pharmaceutical, esp. if the
     pharmaceutical product must be taken on a longer term basis in the
     treatment or prevention of high plasma cholesterol. The accumulation of
     the impurities from the pharmaceuticals of lower purity may cause many
     side effects during the medical treatment. The present invention relates
     to a new industrial process for the isolation of HMG-CoA reductase
     inhibitors using so-called displacement chromatog.
     Use of the invention enables to obtain HMG-CoA reductase
     inhibitors of high purity, with high yields, lower prodn. costs and
     suitable ecol. balance. Crude sodium salt of pravastatin (HPLC purity
     88%) was dissolved in the mobile phase A (distd. water), pH was adjusted
     to 7 with 0.2M aq. NaOH soln. and filtered. The column was equilibrated
     with mobile phase A. The sample obtained in the above manner was fed onto
     the Grom-Sil 120-ODS HE column (particle size 30 11 .mu.m, column size 250
     x 10 mm). The column was washed with the mobile phase B contg. 7% of
     diethylene glycol monobutyl ether in mobile phase A at the flow rate of
     4.5 mL/min. Absorbance was measured at 260 nm, and the 0.5 mL fractions
     were collected with an initial increase in the absorbance. When the
     signal decreased the column was washed with 25 mL of 70% MeOH. The
     fractions obtained were analyzed by the HPLC method. The fractions with a
     purity 99.5% were pooled. In the pooled fractions (7 mL), the HPLC purity
     was 99.8%.
REFERENCE COUNT:
                               THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
=> d 13 ibib abs hitstr tot
     ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
                         2000:210141 CAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         132:241979
TITLE:
                         Process for obtaining HMG-CoA reductase
                         inhibitors of high purity
INVENTOR(S):
                         Grahek, Rok; Milivojevic, Dusan; Bastarda, Andrej
                         Lek Pharmaceutical and Chemical Company D.D., Slovenia
PATENT ASSIGNEE(S):
                         PCT Int. Appl., 25 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,

Page 5 15:18 Print selected from Onli 07/23/2003

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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PATENT NO.
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                                               APPLICATION NO. DATE
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                                                                  19990917
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              KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
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     JP 2002526486
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                              20011130
                                                                  20010316
PRIORITY APPLN. INFO.:
                                            SI 1998-241 A 19980918
                                            WO 1999-IB1553 W 19990917
AB
     Lovastatin, pravastatin, simvastatin, mevastatin, atorvastatin, and
     derivs. and analogs are known as HMG-CoA reductase inhibitors
     and are used as antihypercholesterolemic agents. The majority of them are
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     chem. synthesis. The purity of the active ingredient is an important
     factor for manufg. the safe and effective pharmaceutical, esp. if the
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     treatment or prevention of high plasma cholesterol. The accumulation of
     the impurities from the pharmaceuticals of lower purity may cause many
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     chromatog. Use of the invention enables to obtain HMG
     -COA reductase inhibitors of high purity, with high yields, lower prodn.
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     column size 250 \times 10 mm). The column was washed with the mobile phase B
     contg. 7% of diethylene glycol monobutyl ether in mobile phase A at the
     flow rate of 4.5 mL/min. Absorbance was measured at 260 nm, and the 0.5
     mL fractions were collected with an initial increase in the absorbance.
     When the signal decreased the column was washed with 25 mL of 70% MeOH.
     The fractions obtained were analyzed by the HPLC method. The fractions
     with a purity 99.5% were pooled. In the pooled fractions (7 mL), the HPLC
     purity was 99.8%.
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THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN ACCESSION NUMBER: 1982:449945 CAPLUS DOCUMENT NUMBER: 97:49945

6

REFERENCE COUNT:

Page 6 15:18 Print selected from Onli 07/23/2003

TITLE:

Identification of protein(s) secreted by the

preovulatory ovary which suppresses the follicle

response to gonadotropins

AUTHOR (S): DiZerega, Gere S.; Goebelsmann, Uwe; Nakamura, Robert

Sch. Med., Univ. Southern California, Los Angeles, CA, CORPORATE SOURCE:

90033, USA

SOURCE: Journal of Clinical Endocrinology and Metabolism

(1982), 54(6), 1091-6

CODEN: JCEMAZ; ISSN: 0021-972X

DOCUMENT TYPE: Journal LANGUAGE: English

Ovarian venous blood (5 mL) was collected from women undergoing laparotomy for indications not related to ovarian dysfunction on days 12-14 after the onset of their last menstrual period. Serum was fractionated by (NH4)2SO4 pptn., dialyzed against buffer with 10,000 mol. wt. exclusion membranes, and thereafter sequentially eluted through concanavalin A and Sephadex G-50 columns. The activity of the eluent was assessed as inhibition of ovarian wt. increase and serum 17.beta.-estradiol [50-28-2] levels in 23-day-old, hypophysectomized, diethylstilbestrol-treated rats (HIFR) challenged with human menopausal gonadotropin (hMG) [61489-71-2]. Sephadex G-50 fractions (elution vol./void vol. 1.42-1.55) from patient 1 produced a decrease in ovarian wt. (59 vs. $89.1\ g$) and a decrease in serum 17.beta.-estradiol levels (<25 vs. 215.5 pg/mL). Although peripheral and ovarian venous blood collected from the ovary contralateral to the site of ovulation demonstrated similar Sephadex G-50 elution profiles, when representative fractions were tested by bioassay, no redn. in ovarian wt. or serum 17.beta.-estradiol levels was found. addn., ovarian venous serum from the ovulatory ovary of patients 2 and 3 had a similar Sephadex G-50 elution profile with fractions (elution vol./void vol. = 1.48-1.60) which suppressed rat ovarian wt. and serum 17.beta.-estradiol concns. in the **hMG**-HIFR assay. When active fractions from the G-50 eluents were heated to 56.degree. or trypsin digested, they lost their ability to suppress ovarian wt. and 17.beta.-estradiol secretion in response to hMG stimulation. Estns. of mol. wt. by gel permeation ranged 14,000-18,000 for patients 1-3. Bioassay results from representative fractions obtained by ampholyte displacement chromatog. suggested that the isoelec. point of active material was pH, 5.8-6.5 for patients 1-3. Similarly processed samples from 3 anovulatory patients contained no inhibitory activity in the bioassay. Thus, the identification of a heat- and trypsin-labile substance secreted directly into the venous drainage from the ovary contg. the dominant follicle which suppresses the follicular response to gonadotropins is reported. That this protein is not secreted in large amts. by anovulatory ovaries was evidenced by the failure of the bioassay to detect inhibitory activity in the venous drainage of the contralateral ovary of patients 1-3 as well as the ovarian venous

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ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN

2001:334067 CAPLUS ACCESSION NUMBER:

effluents from 3 anovulatory women.

DOCUMENT NUMBER: 135:225890

TITLE: Chromatographic purification of some

3-hydroxy-3-methylglutaryl coenzyme A reductase

inhibitors

AUTHOR(S): Grahek, R.; Milivojevic, D.; Bastarda, A.; Kracun, M. CORPORATE SOURCE: Lek d.d., Research and Development, Ljubljana, 1526,

Slovenia

SOURCE: Journal of Chromatography, A (2001), 918(2), 319-324

Page 7 15:18 Print selected from Onli 07/23/2003 CODEN: JCRAEY; ISSN: 0021-9673 PUBLISHER: Elsevier Science B.V. DOCUMENT TYPE: Journal LANGUAGE: English The purifn. of pravastatin, simvastatin and lovastatin in the sodium salt or lactone form and of mevastatin in the lactone form by reversed-phase displacement chromatog. is presented. The mobile phases consisted of water or mixts. of water-methanol and water-acetonitrile. Six different displacers were successfully used. Up to 0.14 g of raw sample per g of stationary phase was loaded on a column packed with silica-based octadecyl phase. Crude substances from 85 to 88% chromatog. purity were purified and at least 99.5% purity was achieved. REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN ACCESSION NUMBER: 2000:210141 CAPLUS DOCUMENT NUMBER: 132:241979 TITLE: Process for obtaining HMG-CoA reductase inhibitors of high purity INVENTOR(S): Grahek, Rok; Milivojevic, Dusan; Bastarda, Andrej PATENT ASSIGNEE(S): Lek Pharmaceutical and Chemical Company D.D., Slovenia SOURCE: PCT Int. Appl., 25 pp. CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE ______ ____ _____ ______ WO 1999-IB1553 19990917 WO 2000017182 A1 20000330 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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esp. if the pharmaceutical product must be taken on a longer term basis in

Page 8 15:18 Print selected from Onli 07/23/2003

the treatment or prevention of high plasma cholesterol. The accumulation of the impurities from the pharmaceuticals of lower purity may cause many side effects during the medical treatment. The present invention relates to a new industrial process for the isolation of HMG-COA reductase inhibitors using so-called displacement chromatog. Use of the invention enables to obtain HMG-COA reductase inhibitors of high purity, with high yields, lower prodn. costs and suitable ecol. balance. Crude sodium salt of pravastatin (HPLC purity 88%) was dissolved in the mobile phase A (distd. water), pH was adjusted to 7 with 0.2M aq. NaOH soln. and filtered. The column was equilibrated with mobile phase A. The sample obtained in the above manner was fed onto the Grom-Sil 120-ODS HE column (particle size 30 11 .mu.m, column size 250 \times 10 mm). The column was washed with the mobile phase B contg. 7% of diethylene glycol monobutyl ether in mobile phase A at the flow rate of 4.5 mL/min. Absorbance was measured at 260 nm, and the 0.5 mL fractions were collected with an initial increase in the absorbance. When the signal decreased the column was washed with 25 mL of 70% MeOH. The fractions obtained were analyzed by the HPLC method. The fractions with a purity 99.5% were pooled. In the pooled fractions (7 mL), the HPLC purity was 99.8%.

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